Letter

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Response to Thomas and Baker: the structural adaptation of the brain to training

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In their letter to *TiCS*, Thomas and Baker rightly raise the question of whether training has a causal effect on adult brain structure [1], given that, to date, the question has only received an indirect answer. Although animal [2] and human data [3] strongly suggest that this is the case, the causal relationship has not yet been demonstrated [4].

Specifically, Thomas and Baker discuss three critical issues: (i) replication of findings; (ii) the reliability of voxel-based morphometry (VBM) as a method for investigating structural brain changes; and (iii) the biological nature of the changes in brain structure that are reported.

We agree with Thomas and Baker on the last issue, in that the answer is simply not yet known; hypotheses concerning the morphological cause of brain structure changes observed using VBM form a substantial part of the original review [5].

Regarding the first point, however, we note that Driemeyer *et al.* [6] included an analysis that reported the combined results of the data sets in Draganski *et al.* [7] and Driemeyer *et al.* [6]. A mean effect analysis was used for this purpose, which allowed the authors to combine data from different scanners. This was the first time that two independent cohorts exhibited transient gray matter increase in the exact same area. Moreover, the variability map of Thomas and Baker is not the appropriate approach to summarize the findings of different studies. Their coordinate-based method uses only the location of the peak findings, which might be misleading compared with image-based approaches that make use of the full statistic image [8]. To demonstrate the consistency and robustness of the three juggling studies by May and colleagues, we performed a conjunction analysis comprising all three studies [6,7,9]. We found a consistent cluster in all the studies (Figure 1) that corresponds to the cytoarchitectonic map of the right area hMT/V5 [10], as well as to the average peak of the area hMT [11] that was cited by Thomas and Baker. We note that this finding across different scanners and even different field strengths supports the consistency and reliability of these previous results.

It is important to note, however, that the comparison of MR morphometry studies done at different research centres is currently almost impossible owing to scanner- and site-specific properties. Moreover, at this time, there is still some ambiguity around when morphometric changes can first be detected (days or months) and how long the changes last. Also missing is the validation of studies that analyse the functional impact of these morphometric results.

In summary, we entirely agree with Thomas and Baker that the interpretation of any results using morphometric methods deserves careful consideration. As long as these central issues remain unanswered, information based on clinical-pathophysiological research remains limited. One

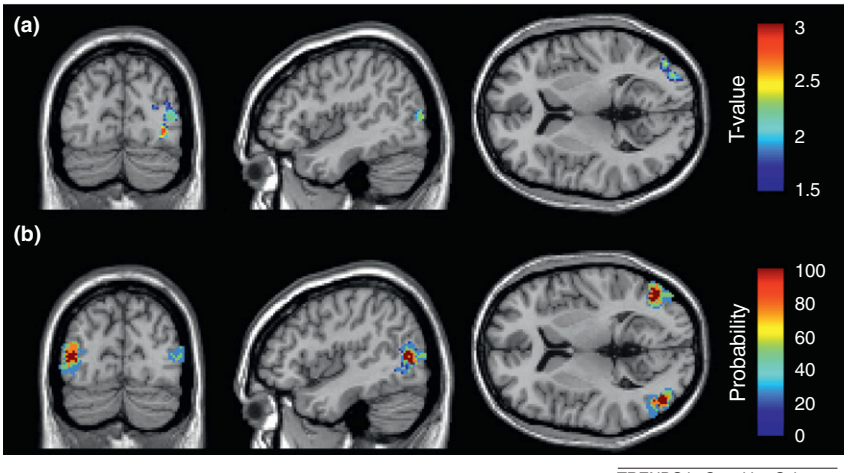

Figure 1. Conjunction analysis to examine effects that are common in three juggling studies [6,7,9]. The location of the three orthogonal slices [xyz coordinates in Montreal Neurological Institute (MNI) space: 46/–78/6 mm] corresponds to the average peak of the area hMT [11]. **(a)** The result is thresholded at $P<0.05$ (corrected for multiple comparisons using the false discovery rate) and overlaid onto a representative single subject brain. **(b)** Probabilistic map of area hOc5 based on delineations in histological sections of ten postmortem brains in MNI space.

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of the great challenges in the future is the validation of morphometric methods as well as the development of reliable means that allow the pooling of data from several scanners and centres. With the application of these methods, MR-based morphometry will become an extremely powerful tool for multicentre and therapeutic trials of several brain diseases.

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